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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/608,463	06/27/2003	James W. Ryan	JR-10,003-US	6428

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EXAMINER	
SLOBODYANSKY, ELIZABETH	
ART UNIT	**PAPER NUMBER**
1652	

DATE MAILED: 12/01/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/608,463	RYAN, JAMES W.	
	Examiner	Art Unit	
	Elizabeth Slobodyansky, PhD	1652	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *05 June 2004 and 17 September 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-22* is/are pending in the application.

4a) Of the above claim(s) *1-6,8,9,11-14,21 and 22* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *7,10 and 15-20* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

The amendment filed June 5, 2004 amending claims 1-5, 7-17 and 19-22 has been entered.

Claims 1-22 are pending.

Election/Restrictions

It is noted that claim 9, dependent from claim 1, should be included in Groups I-II and was recited in Group VI in inadvertent and obvious error.

Applicant's election with traverse of Group VI, claims 7, 10 and 15-20, drawn to a non-coding region of SEQ ID NO:4, in Paper filed June 5, 2004 is acknowledged. The traversal is on the ground(s) that "At the very least, groups II, IV, VI, VIII, X and XI should be examined together. This is because of the linking claims 7, 8, 11, 13 and 22. As noted above, claim 7 now depends from claim 1. It is Applicant's position that claim 7 and claim 1 constitute the same invention. This is because claim 7 is merely directed to a sequence hybridizing to a non-coding region of claim 1. However, even assuming *arguendo* that claim 1 and claim 7 are different inventions, they should be examined together because they are linked together. As noted above, other linking claims include claims 8, I 1, 13, and 22" (Remarks, page 7).

This is not found persuasive because neither claim 1 nor claim 7 are linking with regard to each other. Claim 7 is drawn to any, i.e. naturally-occurring and man made, sequence that hybridizes to a non-coding region of SEQ ID NO:4 whereas claim 1 is drawn to a genomic, i.e. naturally-occurring sequence comprising the non-coding as

well as coding region. The mere fact that claim 7 depends from claim 1 does not render it a linking claim.

Applicants further argue that "It is also Applicant's position that it is unnecessary to examine SEQ ID NO:3 and 4 separately. This is because only two sequences involved and their proximity to each other. Specifically, the two sequences are located in the human chromosome 12q13-q15 region and are contiguous. Thus it would not constitute an undue burden to search both of these sequences" (page 7). This is not persuasive because SEQ ID NO:3 and SEQ ID NO:4 have different structures and functions and encode unrelated proteins with totally different functions and properties. In addition, the search of any of SEQ ID NO:3 or SEQ ID NO:4 is a significant burden because of their length exceeding 150,000 bp.

The requirement is still deemed proper and is therefore made FINAL.

Applicants further elected the species of a splice junction in Paper filed September 17, 2004.

Claims 1-6, 8, 9, 11-14, 21 and 22 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to nonelected Groups I-V and VII-XII, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in Paper filed June 5, 2004.

Claims 7, 10 and 15-20, species of a splice junction, are under examination.

Claim Objections

Claim 7, with dependent claims 10 and 15-20, is objected to as dependent from non-elected claim 1.

Claim 7 is further objected to as reciting non-elected species.

Claim 19 is objected to as reciting "SEQ ID NO3" instead of "SEQ ID NO:3".

Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 7, 10 and 15-20 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claim 7, with dependent claims 10 and 15-20, is drawn to a "nucleic acid molecule of at least 20 nucleotides that specifically hybridizes to a non-coding region of SEQ ID NO:4. Claim 7 encompasses structurally diverse nucleotides because a non-coding region of claim 7 encompasses an intron, a slice junction, a 5'-non-coding region, an expression control element, a transcription factor binding region and a 3'-non-coding region. The claimed molecules are structurally diverse because they

encompass molecules that hybridize to any splice junction of SEQ ID NO:4. Furthermore, the function of the claimed at least 20 nucleotides is not defined (see the 112, 2nd paragraph rejection below).

Therefore, the genus of nucleic acid molecules that comprise these above nucleic acid molecules is a large variable genus with the potentiality of encoding many different proteins and encoding no proteins but having other functions. Therefore, many functionally unrelated nucleic acid molecules are encompassed within the scope of the claim, including partial nucleic acid sequences. The specification does not contain any disclosure of the function of all nucleic acid sequences that hybridize under high stringency to a non-coding region, including a splice junction of SEQ ID NO:4. There are several known splice variants of SEQ ID NO:4 (Sigalas et al. (1996) Nature medicine, 2, 912-917, especially page 913). The specification discloses only splice sites for a single splice variant of SEQ ID NO:4 from which splice junctions of this variant can be gleaned (page 10, Table 2). Moreover, the specification fails to describe any other representative species by any identifying characteristics or properties and fails to disclose the correlation between function and structure common to all members of the genus of splice junctions. Thus, one skilled in the art cannot visualize or recognize the identity of the members of the genus.

One skilled in the art cannot reasonably conclude that the applicant had possession of the claimed invention at the time the instant application was filed.

Claims 7, 10 and 15-20 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a non-coding region of at least 20 nucleotides of SEQ ID NO:4, does not reasonably provide enablement for at least 20 nucleotides that specifically hybridize to a non-coding region, including splice junction, of SEQ ID NO:4 and have no known function. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, how to make and/or use the invention commensurate in scope with these claims.

Factors to be considered in determining whether undue experimentation is required, are summarized in In re Wands 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988). They include (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims.

Claim 7 encompasses nucleic acid molecules having different strictures and undefined functions.

While recombinant, mutagenesis and hybridization techniques are known, it is not routine in the art to screen large numbers of nucleic acid molecules wherein the activity is unpredictable based on the instant disclosure.

One of ordinary skill in the art would not know how to use a nucleic acid without knowing its activity.

Therefore, one of ordinary skill in the art would require guidance, beyond that provided in the specification, in order to make and use a nucleic acid molecule of at least 20 nucleotides that specifically hybridizes to any splice junction of SEQ ID NO:4 and has no known activity in a manner reasonably correlated with the scope of the claims. Without such guidance, the experimentation left to those skilled in the art is undue.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 7, 10 and 15-20 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 7 is drawn to "an isolated nucleic acid molecule of at least 20 nucleotides that specifically hybridizes to a non-coding region of the nucleic acid molecule of claim 1". The term "specifically hybridizes" is not defined in the specification where hybridization are given by non-limiting examples (page 8). Furthermore, the term "splice junction" is not defined in the specification (page 9, line, 32). It can be gleaned that splice junction should comprises junction between intron and exon. As mentioned above the specification teaches 5' and 3' splice sites (Table 2). However, it is not defined how many nucleotides on each side of exon-intron junction it comprises. Furthermore, claim 7 recites a non-coding region that is a splice junction. It is confusing because it can be

construed as directed to only a non-coding, i.e. intron part of a splice junction. Further, claim 7 depends from claim 1 which in its turn is unclear. For example, the metes and bounds of the term "variant" are unclear. It is unclear the difference between a nucleic acid and its "reverse complement". The metes and bounds of the term "complement" are not clearly defined and include fully and partially complementary sequences (page 8, lines 10-17).

Claim 19 depends from claim 18. Claim 18 is drawn to "The solid support of claim 17 wherein said support is a microarray". Claim 19 is drawn to "The solid support of claim 18, wherein said microarray further comprises a plurality of nucleic acid molecules hybridizing to a non-coding region of SEQ ID NO:3 or 4". The limitation in claim 19 appears to be redundant because the microarray comprises a plurality of nucleic acid molecules hybridizing to a non-coding region of SEQ ID NO:4.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 7, 10 and 15 are rejected under 35 U.S.C. 102(b) as being anticipated by Muzny et al.

Muzny et al. (GenBank accession AC025423, March 9, 2000) teach the sequence of human chromosome 12 comprising the sequence of SEQ ID NO:4. Said sequence would hybridize to a fragment thereof that is a non-coding region, including splice junction. To be sequenced and submitted to GenBank database, the DNA should be inserted in a vector that can be considered as a composition comprising said DNA and a carrier.

Claim 15 is included herein because "A kit" can be construed as a preamble that does not limit the scope and has no patentable weight.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 7, 10 and 15-20 are rejected under 35 U.S.C. 103(a) as being unpatentable over Muzny et al. in view of et al.

The teachings of Muzny et al. are outlined above.

Vogelstein et al. (US Patent 5,411,860, GenBank accession NM_002392) teach cloning, functional expression and chromosomal localization of human mouse double minute (MDM2) homolog. They teach cDNA (SEQ ID NO:1) encoding human MDM2

homolog (SEQ ID NO:2) that is 100% identical to the human MDM2 homolog of the instant invention (SEQ ID NO:2). They a labeled probe, they localized the gene encoding said human MDM2 homolog to chromosome 12q12-14 (column 5, lines 2-13; the description of SEQ ID NO:1 in the Sequence Listing).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to use said cDNA to identify the genomic DNA that encodes the human MDM2 homolog of SEQ ID NO:2 on chromosome 12q12-14. The state of the art provides various techniques for obtaining genomic DNA using cDNA probes that are usually labeled. The comparison of genomic and cDNA would result in the identification of non-coding regions. One of ordinary skill in the art would have been motivated to use said non-coding regions or fragments thereof of at least 20 nucleotides for detecting variants of chromosome 12q12-14 from genomic nucleotide samples from an individual, for example. As a matter of convenience a non-coding region such as a splice junction or fragments thereof can be present in a kit or on a solid support. Further, said support can be a microarray according to a customary use of nucleic acid molecules in the art.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Elizabeth Slobodyansky, PhD whose telephone number is 571-272-0941. The examiner can normally be reached on M-F 10:00 - 6:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathapura Achutamurthy, PhD can be reached on 571-272-0928. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

E. Slobodyansky

Elizabeth Slobodyansky, PhD
Primary Examiner
Art Unit 1652

November 24, 2004